

JC03 Rec'd PCT/PTO T1 JAN 2002

FORM PT (REV. 10-2		MMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER				
TRANSMITTAL LETTER TO THE UNITED STATES							
	DESIGNATED/ELECTED	OFFICE (DO/EO/US)	U S APPLICATION NO (If known, see 37 CFR 1 5)				
,	CONCERNING A FILING		10/030810				
INTERN PCT/GB	ATIONAL APPLICATION NO. 00/02678	INTERNATIONAL FILING DATE 12 July 2000 (12.07.00)	PRIORITY DATE CLAIMED 13 July 1999 (13.07.99)				
TITLE	OF INVENTION						
	TRANSFER PIN	146 444	,				
	ANT(S) FOR DO/EO/US Stuart: MOORE David: PEARSON Jon.	athan					
	ELMES, Stuart; MOORE, David; PEARSON, Jonathan Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:						
1. 🛛							
2.							
3. ⊠	This is an express request to promptly be	gin national examination procedures (35 U.S.C.	371(f)).				
4. ⊠	The US has been elected by the expiration	n of 19 months from the earliest claimed priority	y date (PCT Article31).				
5. ⊠	A copy of the International Application a	as filed (35 U.S.C. 371(c)(2)).					
	a. \(\sigma\) is transmitted herewith (required or	nly if not transmitted by the International Bureau	1).				
	b. □ has been transmitted by the Interna						
6.	An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). a. □ is transmitted herewith (required only if not transmitted by the International Bureau). b. □ has been transmitted by the International Bureau.						
7. ⊠	Amendments to the claims of the International Application under PCT Article 19 (35 U.S C. 371(c)(3)). a. □ are attached hereto (required only if not transmitted by the International Bureau). b. □ have been communicated by the International Bureau. c. □ have not been made; however, the time limit for making such amendments has NOT expired.						
	d. ⊠ have not been made and will not be	_	•				
8.		nendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).				
9. 🗆	☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).						
10.	An English language translation of the ar PCT Article 36 (35 U.S.C. 371(C)(5)).	nnexes to the International Preliminary Examina	tion Report under				
Items 11	To 16. Below concern document(s) or	information included:					
11. □ 12. □	11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.						
13.	A,FIRST preliminary amendment.						
	5. W. All IKST promining antendinent.						
14.	4. A SECOND or SUBSEQUENT preliminary amendment.						
15.	A substitute specification.						
16.	A change of power of attorney and/or add	dress letter.					
17.	A computer-readable form of the sequence	ce listing in accordance with PCT Rule 13ter.2 a	and 35 U.S.C.1.821-1.825.				
18. □	A second copy of the published internation	onal application under 35 U.S C. 154(d)(4).					
19.	A second copy of the English language to	ranslation of the international application under	35 U.S.C. 154(d)(4).				
20. ☑ Other items or information: Copy of PCT Published Application w/ International Search Report Copy of International Search Report Copy of International Preliminary Examination Report Express Mail Label No. EL819462341US Date Mailed: January							

531 Rec'd PC 11 JAN 2002

U.S. APPLICATION NO (II known	· SPIPERPIN Q I N	INTERNATIONAL APPLICATION	ı .	ATTORNEY'S DOCKET	NUMBER
1 U / U 5 U 8 L U PCT/GB00/02678				CALCULATIONS PTO USE ONLY	
21. ☑ The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)): Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$1000.00					
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$860.00					
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but but international search fee paid to USPTO (37 CFR 1.445(a)(2)).paid to USPTO \$710.00				:	
International preliminary examination fee paid to USPTO (37 CFR 1.482) But all claims did not satisfy provisions of PCT Article 33(1)-(4) \$690.00					
and all claims satisf	International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) ENTER APPROPRIATE BASIC FEE AMOUNT = 860.00				
, –	_	eclaration later than 20) □ 30	\$860.00	
months from the earliest		` / /	DATE		
CLAIMS Total Claims	NUMBER FILED 35-20=	NUMBER EXTRA	X \$18.00	\$270.00	<u> </u>
Independent Claims	11-3 =	8	X \$80.00	\$640.00	
MULTIPLE DEPENDE		able) 0	+\$270.00	\$270.00	
	TOTAL OF	ABOVE CALCULATION		\$2040.000	
Applicant claims small 1/2.	entity status. See 37 CF	R 1.27. The fees indicated	above are reduced by	\$	
		SUBTOT	AL =	\$2040.00	
Processing fee of \$130.0 months from the earliest		ish translation later than [20 🗌 30	\$	
months from the carriest	claimed priority date (37	TOTAL NATION	IAL FEE =	\$2040.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be				\$	
	opriate coversheet (37 CI	FR 3.28, 3.31). \$40.00 per OTAL FEES ENCLOSE	property +		1
	\$2040.00				
				Amount to be: refunded	\$
				charged	\$
a. ⊠ A check in the a	mount of \$2040.00	To cover the abo	ve fees is enclosed.		
b. Please charge my Deposit Account NoIn the amount of \$To cover the above fees A duplicate copy of this sheet is enclosed.					
1			a salai ah arasa ha na maina d	on anadit ann arrama	arimont to Damonit
c. The commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 23/2825. A duplicate of this sheet is enclosed.					
d. Fees are to be charged to a credit card. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.					
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.					
					0/
	neeh	Then			
SEND ALL CORRESPONDENCE TO SIGNATURE					
WOLF, GREENFIELD & SACKS, P.C. Lawrence M. Green				n	
600 Atlantic Avenue			NAME		
Boston, Massachuset	ts 02210				
Tel: (617) 720-3500			29,384		•
	HERBITA HARRIMINA BININA MININA	III	REGISTRATION NO		
CUSTOMER NUME	2222	·			

page 2 of 2

10/030810

WO 01/03837

PTO/PCT Rec'd 0 3 JUN 2002

LIQUID TRANSFER PIN

The present invention relates to a liquid transfer pin for transferring one or more drops of fluid to a substrate, and to a method of producing such a pin, and in particular, to a liquid transfer pin for producing microarrays of droplets for testing in the field of life sciences, and to a method of producing such a liquid transfer pin.

Molecular biologists have a need to be able to create an array of thousands of different fluidic samples on a microscope slide o7r other substrate. Such arrays are typically prepared using a liquid transfer tool. The tip of the liquid transfer tool is dipped into a relatively large volume source of the sample liquid (typically 5 to 40 microlitres) to pick up a droplet on the tip of the tool. The tip of the liquid transfer tool is then contacted with the substrate to transfer the droplet to the substrate. In the case that an array comprising dots of different sample fluids is to be prepared, the above procedure is repeated the necessary times to give the desired number of spots of the first sample fluid; the tool is then cleaned; and then the whole procedure is repeated for each of the plurality of sample fluids.

These liquid transfer tools are typically combined in groups attached to a common base to provide a multi-pin liquid transfer tool so that a plurality of droplets can be transferred to the substrate in a single movement of the base to form an array.

The array-forming process can be further expedited by providing the liquid transfer tool with a reservoir which

is connected to the tip of the liquid transfer tool and which can hold enough of the sample fluid for transferring a plurality of droplets to one or more substrates. The provision of such a reservoir greatly reduces the number of moves the liquid transfer tool needs to make between the substrate(s) and the sample fluid source.

Monolithic liquid transfer tools prepared by the micromachining of solid pins are known. A slot extending from the tip of the pin is cut into the pin using wire electronic discharge machining (EDM). The smallest slots that have been produced with this technology are slots having a width in the range of 30 to 40 microns.

There has however been a demand for a liquid transfer tool having smaller slot widths for creating an array of droplets of yet smaller diameter in order to create an array of yet greater droplet density. This demand has been somewhat met by modifying the monolithic liquid transfer pins mentioned above by plastic deformation of the tip of the pin to reduce the width of the slot at the tip of the pin from the machined width of 30 to 40 microns to a smaller width.

Such plastic deformation has generally been carried out in the following ways with reference to Figures 7(a), 7(b), 8(a) and 8(b) of the accompanying drawings. According to one approach, the pin is machined with the aim of producing a perfect point as shown in Figure 7(a). The pin is then deformed in the manner generally shown in Figure 7(b) when the tip of the pin is first tapped on the substrate. This method is particularly uncontrolled

and results in some pins which become deformed to the extent that they no longer work.

According to a another approach, the pin is machined to have an increased tip diameter as shown in Figure 8(a). The pin is then plastically deformed before use by a crimping operation or with a screw arrangement to produce an axially tapered slot having a narrowed exit at the tip.

However, the inventors of the present invention have found that these plastic deformation processes are inherently inconsistent resulting in pins of varying slot widths and tip diameters. As mentioned above, multi-pin liquid transfer tools require a group of liquid transfer pins having uniform dimensions in order to produce an array of uniformly-sized droplets, and a lot of time and effort is therefore required to select pins having matching dimensions.

An aim of the present invention is to provide a liquid transfer pin and a method of producing a liquid transfer pin which at least partially resolves the above-mentioned problems in the prior art.

According to a first aspect there is provided a method of producing a liquid transfer pin having a tip and defining a slot extending from the tip for transferring one or more drops of a fluid to a substrate, the slot comprising an elongate outlet portion extending from the tip and a reservoir portion connected to a distal end of the outlet portion and having a larger cut-out volume than that of the outlet portion, said method comprising the step of producing the pin by a non-deformation process, such as

cutting, wherein the width of the slot at the tip of the pin directly produced by the non-deformation process is no more than 20 microns.

According to a second aspect of the present invention, there is provided a method of producing a liquid transfer pin having a tip and defining a slot extending from the tip for transferring one or more drops of a fluid to a substrate, the slot comprising an elongate outlet portion extending from the tip and a reservoir portion connected to a distal end of the outlet portion and having a larger cut-out volume than that of the outlet portion, said method comprising the step of cutting the slot into a tip of a solid pin, wherein the width of the outlet portion at the tip is no more than 20 microns directly after cutting.

According to a third aspect of the present invention, there is provided a method of producing a liquid transfer pin having a tip and defining a slot extending from the tip for transferring one or more drops of a fluid from the tip to a substrate, the slot comprising an elongate outlet portion extending from the tip and a reservoir portion connected to a distal end of the outlet portion and having a larger cut-out volume than that of the outlet portion, said method comprising using copper vapour laser cutting to form the slot in a tip of a solid pin.

According to a fourth aspect of the present invention there is provided a liquid transfer pin produced by any of the above-described methods.

According to a fifth aspect of the present invention there is provided a liquid transfer pin for transferring one or more drops of a fluid to a substrate from a tip thereof, the liquid transfer pin defining a slot extending from the tip, wherein the slot comprises an elongate outlet portion extending from the tip, and a reservoir portion connected to a distal end of the outlet portion, the width of the reservoir portion being greater than the width of the outlet portion at the point where it is connected to the outlet portion.

According to a sixth aspect of the present invention, there is provided a liquid transfer pin for transferring one or more drops of a fluid to a substrate from a tip thereof, the liquid transfer pin defining a slot extending from the tip, wherein the slot comprises an outlet portion extending from the tip and having a substantially axially uniform width, and a reservoir portion connected to the distal end of the outlet portion and having a substantially axially uniform width, the width of the outlet portion being less than the width of the reservoir portion.

According to a seventh aspect of the present invention, there is provided a liquid transfer pin for transferring one or more drops of a fluid to a substrate from a tip thereof, the liquid transfer pin defining a slot extending from the tip, wherein the slot comprises an outlet portion extending from the tip and having a substantially axially uniform width of less than 20 microns, and a reservoir portion connected to a distal end of the outlet portion and having a larger capacity than the outlet portion.

According to an eighth aspect of the present invention, there is provided a multi-pin liquid transfer tool comprising a plurality of liquid transfer pins as described above.

According to a ninth aspect of the present invention, there is provided a method of producing a multi-pin liquid transfer tool by attaching a plurality of liquid transfer pins to a common base, each liquid transfer pin having a tip and defining a slot extending from the tip, wherein each liquid transfer pin is produced by cutting a slot into a tip of a solid pin, the width of the slot at the tip being less than 20 microns directly after cutting.

According to an tenth aspect of the present invention, there is provided a method of producing a multi-pin liquid transfer tool by attaching a plurality of liquid transfer pins to a common base, each liquid transfer pin having a tip and defining a slot extending from the tip, wherein each liquid transfer pin is produced by cutting a slot into a tip of a solid pin by copper vapour laser cutting.

According to a eleventh aspect of the present invention, there is provided a multi-pin liquid transfer tool produced by either of the above-described methods.

According to a twelfth aspect of the present invention, there is provided a method of producing an ordered array of spots on a substrate using a liquid transfer pin or a multi-pin liquid transfer tool as described above.

According to a thirteenth aspect of the present invention there is provided a method of transferring one or more drops of liquid to one or more substrates using a liquid transfer pin, wherein the liquid transfer pin has a tip and defines a slot extending from the tip and is produced by cutting a slot into a tip of a solid pin, wherein the width of the slot at the tip is no more than 20 microns directly after cutting.

According to a fourteenth aspect of the present invention, there is provided a method of transferring one or more drops of liquid to one or more substrates using a liquid transfer pin, wherein the liquid transfer pin has a tip and defines a slot extending from the tip and is produced by cutting a slot into a tip of a solid pin by copper vapour laser cutting.

According to a preferred embodiment of the above-described aspects of the present invention, the slot extends right through the pin in a direction perpendicular to the longitudinal axis of the pin. In an alternative embodiment, all or a part of the slot may only extend partially through the pin in a direction generally perpendicular to the longitudinal axis of the pin, i.e. may only be open on one side in a direction perpendicular to the axis of the pin.

Embodiments of the present invention will be described hereunder, by way of example only, with reference to the accompanying drawings, in which:-

Figure 1 shows a schematic cross-sectional view of the working end of a liquid transfer pin according to an embodiment of the present invention;

Figure 2 is a graph showing the performance of liquid transfer pins according to embodiments of the present invention with respect to consistency of volume dispensed;

Figure 3 shows a schematic perspective view of the working end of the liquid transfer pin shown in cross-section in Figure 1; and

Figures 4(a) and 4(b) are shematic cross-sectional views taken through lines A-A and B-B in Figure 3, respectively.

Figures 5(a) and 5(b) are cross-sectional views of the kind shown in Figures 4(a) and 4(b) for an alternative embodiment of the liquid transfer pin according to the present invention.

Figure 6 shows a multi-pin liquid transfer tool according to the present invention.

Figures 7 and 8 schematically show the plastic deformation processes used in the prior art.

Figures 9(a) and 9(b) are schematic cross-sections of an alternative embodiment of a liquid transfer pin according to the present invention, taken perpendicular to the longitudinal axis of the pin.

A liquid transfer pin having the geometry generally shown in Figures 1 and 3 is produced according to the following method. A 5mm diameter solid bar of 17-04ph stainless steel is turned, where necessary, and sharpened at one

end to produce a tapered solid pin having the desired dimensions. Copper vapour laser cutting is then used to cut a slot 1 in the tip of the solid pin 6 which extends from the tip 8 of the pin 6 in a direction substantially parallel to the longitudinal axis of the pin 6. As shown in Figures 3, 4(a) and 4(b), the slot extends right though the pin in a direction perpendicular to the longitudinal axis of the pin 6 (i.e. the direction shown by the arrows in Figures 4(a) and 4(b)).

However, as mentioned above, the present invention is not limited to pins in which the slot extends right through the pin, but includes pins in which the outlet portion and/or the reservoir portion only partially extend through the pin in a direction perpendicular to the longitudinal axis of the pin, i.e. are only open on one side in a direction perpendicular to the longitudinal axis of the pin. Figures 9(a) and 9(b) are schematic cross-sectional views of a liquid transfer pin according to the present invention having a slot comprising an outlet portion 20 and a reservoir portion 22 which only extend partially through the pin in a direction generally perpendicular to the longitudinal axis of the pin. Such an alternative construction can be advantageous in the cases of pins having particularly small tip diameters, since it provides the pin with increased mechanical strength against deformation upon use.

The slot comprises an outlet portion 2 having a substantially axially uniform width and a reservoir portion 4 having a substantially axially uniform width which is larger than that of the outlet portion 2.

The term "substantially axially uniform width" refers to the feature that the width of the respective portion of the slot is substantially uniform along the longitudinal (axial) length of the respective portion of the slot, i.e. from the proximal end to the distal end of the respective portion of the slot.

As shown in the cross-sections shown in Figures 4(a) and 4(b), the slot produced by copper vapour laser cutting has a width which is slightly tapered in a direction generally perpendicular to the axis of the transfer pin, i.e. the direction shown by the arrows in Figures 4(a) and 4(b). In the case of such a slot whose width is not uniform in а direction generally perpendicular to the longitudinal axis of the pin, the term "width" refers to the average width respective portion of the slot in the direction shown by the arrows shown in Figures 4(a) and 4(b). mentioned above, the average width of the respective portions of the slot is nevertheless substantially uniform along the axial length of the respective portions of the slot, i.e. from the proximal end to the distal end of the respective portions of the slot.

According to an alternative embodiment, the width of the outlet portion and the reservoir portion of the slot are, as shown in Figures 5(a) and 5(b), also uniform in the direction perpendicular to the axis of the pin, i.e. the direction shown by the arrows in Figures 5(a) and 5(b). In this alternative embodiment, the opposing walls of the outlet portion 2 and reservoir portion 4 are thus substantially parallel to each other.

The copper vapour laser cutting is carried out follows. The solid pin is secured on a mount in the path of the laser beam. The mount is moveable in x and y directions perpendicular to each other and perpendicular to the path of the laser beam. The beam of the laser is focussed down to a dot size of about 5 microns to achieve a sufficient power density to vaporise the material of The laser is then pulsed whilst solid pin. displacing the pin in the x and y directions by moving the mount to successively vaporise and remove a surface layer of dimensions corresponding to those of the desired slot. This process is repeated to remove successive surface layers until the pin has been cut right through to leave a slot of the desired dimensions in the tip of the pin.

In the case of producing a pin in which the slot only partially extends through the pin in a direction generally perpendicular to the longitudinal axis of the pin, the laser cutting is only continued until a slot of the desired depth has been cut.

One of the advantages of copper vapour laser cutting is that the pulsing can be carried out at a high frequency, whereby a large amount of material can be vaporised and eliminated in a short period of time. This reduces the time required to produce the slot of desired shape.

The geometry of the resulting monolithic liquid transfer pin 10 is generally shown in Figures 1, 3, 4(a) and 4(b). The outlet portion 2 preferably has a width, w of no more than 20 microns, preferably in the range of 10 to 20 microns, and further preferably in the range of 10 to 15 microns; and the reservoir portion preferably has a

width, W in the range of 50 to 300 microns, such as about 100 microns. The length, I of the outlet portion 2 is preferably minimised whilst retaining a sufficient wall thickness "t" to prevent plastic deformation upon use of the liquid transfer pin. It is preferably minimised because it is preferred that the volume of the outlet portion is neglible compared to the volume of the reservoir portion. The length of the reservoir portion is preferably in the range of 300 to 2000 microns, such as about 1000 microns.

The working end of the liquid transfer pin shown in Figures 1 and 3 is smoothly tapered towards the tip. Alternatively, it may be tapered in a step-wise manner or not tapered at all.

Furthermore, as shown in Figures 4 and 5 the liquid transfer pin shown in Figures 1 and 3 has a generally circular cross-sectional symmetry. The tip of the liquid transfer pin is squared off and preferably has a diameter in the range of 50 to 200 microns, such as 100, 150 or 200 microns. However, the present invention is not limited to liquid transfer pins having a circular cross-sectional symmetry, and the present invention may be applied to pins having non-circular cross-sectional symmetry such as a tapered or non-tapered thin bladeshaped pin having a generally rectangular cross-section.

Since the resultant liquid transfer pin has the required small dimensions without having to subject the liquid transfer pin to subsequent plastic deformation, liquid transfer pins produced according to this method have consistent dimensions. This consistency means that the liquid transfer pin of the present invention is

particularly useful for producing a multi-pin liquid transfer tool as schematically shown in Figure 6 to be used for simultaneously creating an array of a large number of small droplets of uniform size. In Figure 6, a plurality of liquid transfer pins 10 having working ends as shown in Figures 1 and 3 are orderly arranged on a common base 12, such that the tips of the plurality of liquid transfer pins lie in a single horizontal plane.

The liquid transfer pin of the present invention is used in the conventional manner. The liquid transfer pin is dipped into a source of the sample fluid whereby the outlet portion and reservoir portions become at least partially filled with the sample fluid. The tip of the liquid transfer pin is then tapped against the substrate on which the array is to be formed by relative movement of the tip of the pin towards the substrate to transfer a droplet of the sample fluid from the tip of the liquid transfer pin to the substrate. The tip of the liquid transfer pin is then repeatedly tapped at different portions of the surface of the substrate to form an ordered array of spots on the surface of the substrate.

The liquid transfer pin generally shown in Figures 1 and 3 exhibits excellent performance with respect to consistency of droplet volume with increasing spot number, as shown in the graph in Figure 2. The intensity given on the y-axis is directly proportional to the volume of the droplet dispensed on the substrate. As can be seen from the graph, the volume dispensed is substantially consistent until the very last few spots with a very sharp reduction in dispensed volume for those last few spots. This is in contrast to conventional liquid transfer pins in which the tail-off is much

shallower whereby the dispensed volume is consistent for a smaller proportion of the total number of spots.

CLAIMS

- 1. A method of producing a liquid transfer pin having a tip and defining a slot extending from the tip for transferring one or more drops of a fluid to a substrate, the slot comprising an elongate outlet portion extending from the tip and a reservoir portion connected to a distal end of the outlet portion and having a larger cutout volume than that of the outlet portion, said method comprising the step of cutting the slot into a tip of a solid pin, wherein the width of the outlet portion at the tip is no more than 20 microns directly after cutting.
- 2. A method of producing a liquid transfer pin according to claim 1 wherein the width of the slot at the tip is between 10 and 20 microns directly after cutting.
- 3. A method of producing a liquid transfer pin according to claim 1 or claim 2 wherein the outlet portion of the slot has a substantially axially uniform width.
- 4. A method of producing a liquid transfer pin according to claim 3 wherein the reservoir portion of the slot has a substantially axially uniform width larger than that of the outlet portion.
- 5. A method of producing a liquid transfer pin according to claim 1 wherein the liquid transfer pin is at least partially tapered towards the tip.

6. A method of producing a liquid transfer pin according to any preceding claim wherein the cutting is copper vapour laser cutting.

- 7. A method of producing a liquid transfer pin having a tip and defining a slot extending from the tip for transferring one or more drops of a fluid from the tip to a substrate, the slot comprising an elongate outlet portion extending from the tip and a reservoir portion connected to a distal end of the outlet portion and having a larger cut-out volume than that of the outlet portion, said method comprising using copper vapour laser cutting to form the slot in a tip of a solid tapered pin.
- 8. A method according to claim 7 wherein the width of the slot at the tip is no more than 20 microns.
- 9. A method according to claim 8 wherein the width of the slot at the tip is in the range of 10 to 20 microns.
- 10. A method according to any one of claims 7 to 9 wherein the elongate outlet portion has a substantially axially uniform width.
- 11. A method according to claim 10 wherein the reservoir portion has a substantially axially uniform width larger than that of the outlet portion.
- 12. A method according to claim 7 wherein the liquid transfer pin is at least partially tapered towards the tip.

13. A method according to claim 7 wherein the tip of the liquid transfer pin has a circular cross-section with a diameter in the range of 50 to 200 microns.

- 14. A liquid transfer pin produced by a method according to any of claims 1 to 13.
- 15. A liquid transfer pin for transferring one or more drops of a fluid to a substrate from a tip thereof, the liquid transfer pin defining a slot extending from the tip, wherein the slot comprises an elongate outlet portion extending from the tip, and a reservoir portion connected to a distal end of the outlet portion, the width of the reservoir portion being greater than the width of the outlet portion at the point where it is connected to the outlet portion.
- 16. A liquid transfer pin according to claim 15 wherein the width of the outlet portion at the tip is no more than 20 microns.
- 17. A liquid transfer pin according to claim 16 wherein the width of the outlet portion at the tip is in the range of 10 to 20 microns.
- 18. A liquid transfer pin according to any of claims 15 to 17 wherein the outlet portion has a substantially axially uniform width.
- 19. A liquid transfer pin according to any of claims 15 to 18 wherein the reservoir portion has a substantially axially uniform width.

20. A liquid transfer pin for transferring one or more drops of a fluid to a substrate from a tip thereof, the liquid transfer pin defining a slot extending from the tip, wherein the slot comprises an outlet portion extending from the tip and having a substantially axially uniform width, and a reservoir portion connected to a distal end of the outlet portion and having a substantially axially uniform width, the width of the outlet portion being less than the width of the reservoir portion.

- 21. A liquid transfer pin according to claim 20 wherein the width of the outlet portion is no more than 20 microns.
- 22. A liquid transfer pin according to claim 21 wherein the width of the outlet portion is in the range of 10 to 20 microns.
- 23. A liquid transfer pin for transferring one or more drops of a fluid to a substrate from a tip thereof, the liquid transfer pin defining a slot extending from the tip, wherein the slot comprises an outlet portion having a substantially axially uniform width of less than 20 microns, and a reservoir portion connected to a distal end of the outlet portion and having a larger capacity than the outlet portion.
- 24. A liquid transfer pin according to claim 23 wherein the width of the outlet portion is in the range of 10 to 20 microns.

25. A liquid transfer pin according to claim 24 wherein the reservoir portion also has a substantially axially uniform width.

- 26. A multi-pin liquid transfer tool comprising a plurality of liquid transfer pins according to any of claims 14 to 25 attached to a common base.
- 27. A method of producing a multi-pin liquid transfer tool by attaching a plurality of liquid transfer pins to a common base, each liquid transfer pin having a tip and defining a slot extending from the tip, wherein each liquid transfer pin is produced by cutting a slot into a tip of a solid pin, the width of the slot at the tip being less than 20 microns directly after cutting.
- 28. A method of producing a multi-pin liquid transfer tool by attaching a plurality of liquid transfer pins to a common base, each liquid transfer pin having a tip and defining a slot extending from the tip, wherein each liquid transfer pin is produced by cutting a slot into a tip of a solid pin by copper vapour laser cutting.
- 29. A multi-pin liquid transfer tool produced by the method defined in claim 27 or claim 28.
- 30. A method of producing an ordered array of spots on a substrate using a liquid transfer pin according to any one of claims 15 to 25 or a multi-pin liquid transfer tool according to claim 26 or claim 29.
- 31. A method of producing an ordered array of spots according to claim 30 wherein the diameter of the spots is in the range of 50 to 200 microns.

32. A method of transferring one or more drops of liquid to one or more substrates using a liquid transfer pin, wherein the liquid transfer pin has a tip and defines a slot extending from the tip and is produced by cutting a slot into a tip of a solid pin, wherein the width of the slot at the tip is no more than 20 microns directly after cutting.

- 33. A method of transferring one or more drops of liquid to one or more substrates using a liquid transfer pin, wherein the liquid transfer pin has a tip and defines a slot extending from the tip and is produced by cutting a slot into a tip of a solid pin by copper vapour laser cutting.
- 34. A liquid transfer pin substantially as hereinbefore described with reference to any of Figures 1 and 3 to 5 of the accompanying drawings.
- 35. A multi-pin liquid transfer tool substantially as hereinbefore described with reference to Figure 6 and any of Figures 1 and 3 to 5 of the accompanying drawings.

(19) World Intellectual Property Organization International Bureau

(43) International Publication Date 18 January 2001 (18.01.2001)

PCT

(10) International Publication Number WO 01/03837 A1

(51) International Patent Classification7:

B01L 3/02

(21) International Application Number: PCT/GB00/02678

(22) International Filing Date:

12 July 2000 (12.07.2000)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 9916406.3

13 July 1999 (13.07.1999)

(71) Applicants (for all designated States except US): BIOROBOTICS LIMITED [GB/GB]; Bennell Court, Comberton, Cambridge CB3 7DS (GB). CAMBRIDGE UNIVERSITY TECHNICAL SERVICES LIMITED [GB/GB]; The Old Schools, Trinity Lane, Cambridge CB2 1TS (GB).

(72) Inventors: and

(75) Inventors/Applicants (for US only): ELMES, Stuart,

Antony [GB/GB]; BioRobotics Limited, Bennell Court, Comberton, Cambridge CB3 7DS (GB). MOORE, David, Frank [GB/GB]; Trinity Hall, Cambridge CB2 1TJ (GB). PEARSON, Jonathan [GB/GB]; 4 Babingley Close, Watlington, Norfolk PE33 OTR (GB).

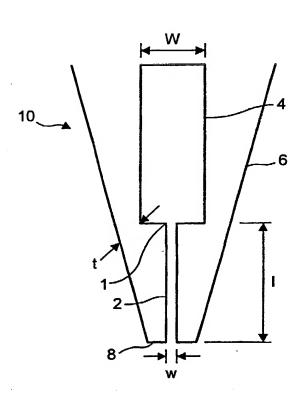
- (74) Agents: DRIVER, Virginia, Rozanne et al.; Page White & Farrer, 54 Doughty Street, London WC1N 2LS (GB).
- (81) Designated States (national): GB, JP, US.
- (84) Designated States (regional): European patent (AT, BE, -CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published:

With international search report.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

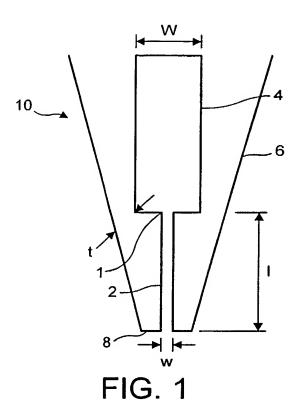
(54) Title: LIQUID TRANSFER PIN



(57) Abstract: A method of producing a liquid transfer pin (10) having a tip (8) and defining a slot (1) extending from the tip (8) for transferring one or more drops of a fluid to a substrate, the slot comprising an elongate outlet portion (12) extending from the tip (8) and a reservoir portion (4) connected to a distal end of the outlet portion and having a larger cut-out volume than that of the outlet portion, said method comprising the step of cutting the slot into a tip of a solid pin, wherein the width of the outlet portion at the tip is no more than 20 microns directly after cutting.



1/4



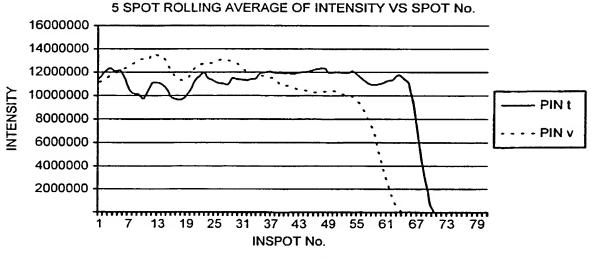
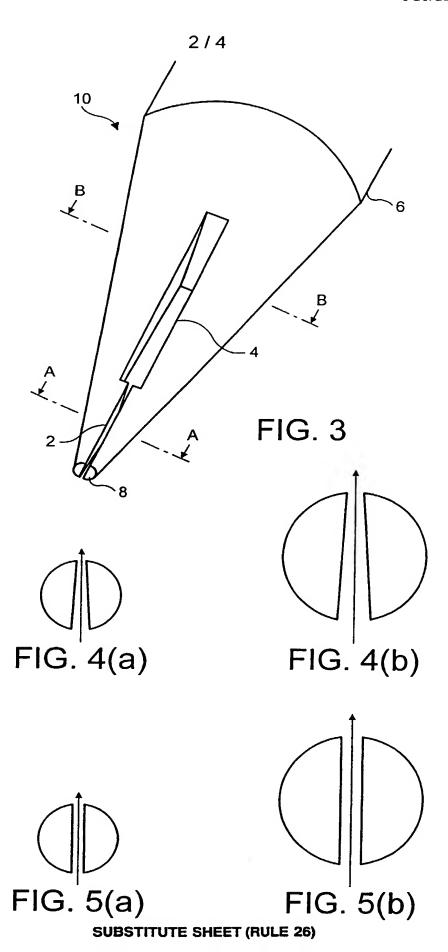
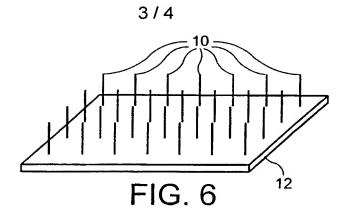


FIG. 2

SUBSTITUTE SHEET (RULE 26)





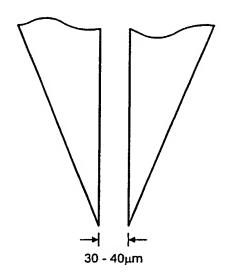


FIG. 7(a)

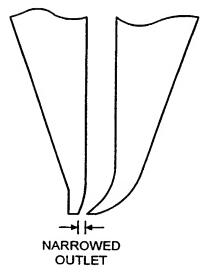


FIG. 7(b)

SUBSTITUTE SHEET (RULE 26)

4/4

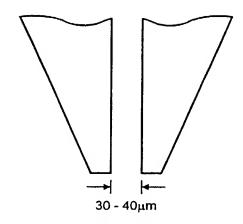


FIG. 8(a)

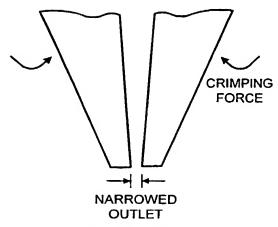


FIG. 8(b)

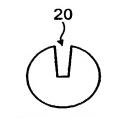


FIG. 9(a)

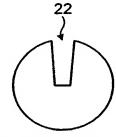


FIG. 9(b)

Attorney Docket No. B01104/70002 LMG

DECLARATION FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

LIQUID TRANSFER PIN

the specification of which is attached hereto unless the following is checked:

- [X] International Application No. PCT/GB00/02678, which was filed on July 12, 2000, and which entered the U.S. National Phase, as Application No. 10/030,810, bearing Attorney Docket No. B01104/70002.
- I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.
- I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56.
- I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or section 365(a) of any PCT International application designating at least one country other than the United States listed below and have also identified below any foreign application for patent or inventor's certificate or PCT International application having a filing date before that of the application on which priority is claimed:

Prior Foreign PCT International Application(s) and any priority claims under 35 U.S.C. §§119 and 365(a),(b):

				imed
9916406.3 (Number)	Great Britain (Country-if PCT, so indicate)	July 13, 1999 (DD/MM/YY Filed)	[X] YES	NO
(Number)	. (Country-if PCT, so Indicate)	(DD/MM/YY Filed)	[]	[] NO
(Number)	(Country-If PCT, so Indicate)	(DD/MM/YY Filed)	[] YES	[] NO

Docket No.: B01104/70002 LMG

Page 2

I hereby claim the benefit under Title 35. United States Code, §119(e) of any United States provisional application(s) listed below:

(Application Number)	(filling date)
(Application Number)	(filing date)

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s), or §365(c) of any PCT International application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

(Application No.)		(filing date)	(status-patented, pending, abandoned)	
(Application No.)		(filing date)	(status-patented, pending, abandened	
PCT International Appl	ications designat	ing the United Stat	tes:	
<u>-</u>				
(PCT Appl. No.)	(U.S. Ser. No.)	(PCT filing date)	(status-patented, pending, abandoned)	

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

	Robert M. Abrahamsen	40,886	Steven J. Henry	27,900	Randy J. Pritzker	_35,986
	Konstantinos Andrikopoulos	48,915	Jason M. Honeyman	31,624	Edward J. Russavage	43,069
	Eric Amundsen	46,518	Robert E. Hunt	39,231	Robert A. Skrivanek, Jr.	41,316
	John N. Anastasi	37,765	Peter C. Lando	34,654	Alan W. Steele	45,128
	Ilan Berzilay	46,540_	M. Brad Lawrence	47,210	Mark Steinberg	40,829
	Carole Boelitz	48,958	Helen C. Lockhart	39,248	Joseph Teja, Jr.	45,157
•	Gary S. Engelson	35,128	Matthew B. Lowrie	38,228	Maria A. Trevisan	48,207
١	Neil P. Ferraro	39,188	William R. McClellan	29,409	John R. Van Amsterdam	40,212
•	Thomas G. Field III.	45,596	Daniel P. McLoughlin	46.066	Robert H. Walat	46,324
	Stephen R. Finch	42,534	Chantal Morgan	48,825	Kristin D. Wheeler	43,583
	Edward R. Gates .	31,616	James H. Morris	34,681_	Lisa E. Winsor	44,405
	Richard F. Giunta	36,149	Timothy J. Oyer	36,628	David Wolf	17,528 36,971
	Lawrence M. Green	29,384	Edward F. Perlman	28,105	Douglas R. Wolf	36,971
	George L. Greenfield	17,756	Elizabeth R. Plumer	36,637		-
	James M. Hanifin, Jr.	39,213	Michael J. Pomianek	46,190		
				_		

43

Docket No.: B01104/70002 LMG

Page 3

Address all telephone calls to Lawrence M. Green at telephone no. (617) 720-3500. Address all correspondence to:

Lawrence M. Green c/o Wolf, Greenfield & Sacks, P.C., Federal Reserve Plaza 600-Atlantic Avenue Boston, MA 02210-2211

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

inventor's signature

Full name of second or joint inventor: Stuart Antony Elmes
Citizenship: Great Britain

Citizenship:

Residence: St Catharine's Farmhouse, 57 High St, Coton, Cambridge CB3 7PL
Post Office Address: St Catharine's Farmhouse, 57 High St, Coton, Cambridge CB3 7PL

Inventor's signa

Full name of first inventor. David Frank Moore

Citizenship: Great Britain
Residence: Trinity Hall, Cambridge CB2 1TJ, Great Britain
Post Office Address: Trinity Hall, Cambridge CB2 1TJ, Great Britain

Inventor's signature

Full name of first inventor: Jonathan Pearson

Great Britain

Residence: 25 Princess Avenue, March, PE15 9SQ

Post Office Address: 25 Princess Avenue, March, PE15 9SQ